

### **REMARKS**

Claims 1-8 and 10-15 are pending with claims 10-15 having been withdrawn from further prosecution as being drawn to a non-elected invention. Applicants reserve the right to pursue these claims in a later filed application claiming the benefit of priority to the above-identified application. Claims 1, 6 and 8 have been amended. Support for the amendments can be found throughout the application as filed. In particular, support for the amendment to claim 1 can be found at, for example, page 18, line 29 through page 19, line 4; page 24, line 26 through page 25, line 31. Claims 6 and 8 have been amended to correct obvious typographical errors in their presentation in Applicants' previous response. Support for the amendment to claims 6 and 8 can be found in original claims 6 and 8 as filed. Accordingly, the amendments do not raise any issue of new matter.

Applicants thank Examiner Clow for extending a personal interview on August 21, 2006, to Applicants' representatives and to Dr. Christophe Schilling, during which amendments were discussed that the Examiner indicated could be viewed favorably. The above amendments and remarks are believed to be consistent with the discussions during the interview.

### **Rejections Under 35 U.S.C. § 101**

Applicants respectfully traverse the rejection of claims 1-8 under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. The Office alleges that the claimed invention must provide a practical application which requires either transformation of a physical object to a different state or thing or a useful, concrete and tangible result. The Office cites to *State Street* and to the Interim Guidelines published November 2005 in support of the assertion that the claims merely encompass *in silico* data manipulation with no specific output that is useful, concrete and tangible. In response to Applicants' remarks, the Office appears to conclude that the process of determining reaction sets that can be used to produce cellular metabolites of interest lacks a practical application, or that predicting a design for re-engineering an organism fails to transform a physical object into a different state or thing.

As discussed during the personal interview with Examiner Clow, Applicants respectfully submit that the law is clear with respect to the statutory criteria required for computer related inventions. Claimed subject matter does not require transformation of an article or physical object into a different state or thing in order to satisfy the requirements of §101. Further, as discussed, Applicants respectfully submit that the claimed method inherently recites production, or output, of an altered network because the steps of the claimed method determine whether deleted reaction sets diminish the capability of the network to produce an output metabolite. Deleting the reaction sets results in an altered network. Nevertheless, Applicants have rewritten these steps to explicitly recite elimination of an internal reaction flux to produce an altered network and determination of whether the eliminated reaction fluxes constitute a minimal deletion set because they diminish the capability of the altered network to produce an output metabolite. In light of these amendments, Applicants submit that this ground of rejection is moot and its withdrawal is respectfully requested.

If the Office insists on maintaining the above rejection under §101, Applicants respectfully remind the Office of the recent authority pointed out during the personal interview held August 21, 2006, which overrules rejections similar to the instant rejection (*In re Lundgren*, B.P.A.I. Case Nos. 2003-2088 (Sept. 28, 2005) (*Per Curium*)). The claimed Lundgren invention was directed to a method of compensating a manager. *Id.*, slip op. at p.1. The Examiner rejected the claimed invention for being directed to non-statutory subject matter allegedly because:

[B]oth the invention and the practical application to which it is directed to be outside the technological arts, namely an economic theory expressed as a mathematical algorithm without the disclosure or suggestion of computer, automated means, apparatus of any kind.

*Id.* slip op. at p.4 (emphasis added).

The requirement for a computer, an automated means or an apparatus in *Lundgren* is similar to the instant requirement for an alleged transformation and, in *Lundgren*, was directly related to the Office's conclusion that the claimed invention was not required to interact with a computer. *In re Lundgren* dispelled any notion for requiring such physical embodiments to exist when the court stated:

In *Musgrave*, the court reversed a rejection under 35 U.S.C. § 101 that the claims under review therein were non-statutory because it disagreed with the Board that “these claims . . . are directed to non-statutory processes merely because some or all of the steps therein can also be carried out in or with the aid of the human mind or because it may be necessary for one performing the processes to think.”

*In re Lundgren*, slip op. at p.7 (emphasis added, citations omitted).

Therefore, the Board of Appeals and Interferences of the U.S. Patent and Trademark Office has overturned rejections attempting to require method claims to include physical embodiments such as computer interactions or physical transformations similar to the instant requirement for a physical transformation. *Id.* This decision by the U.S.P.T.O. negates any rejection based on the alleged requirement for a physical embodiment, such as the above rejection requiring a physical transformation.

Further, with respect to the assertions that the claimed subject matter fails to meet the practical application test of *State Street*, or its interpretation set forth in the M.P.E.P., or as now articulated in the Interim Guidelines, published November 22, 2005, Applicants further agreed that any inquiry into the patentability of the claimed subject matter is necessarily framed under *State Street*, where the inquiry is whether the claimed invention has a practical application (149 F. 3d 1368, 1373-74 (Fed. Cir. 1998)). The *State Street* inquiry serves to exclude subject matter that falls under one of three judicial exceptions to patentability. The claimed invention satisfies the practical application test set forth in *State Street*, which requires a useful, concrete and tangible result because, as explained previously, the claimed invention can be used to produce biochemical products of interest; the method identifies a point of interdiction that can be targeted for therapeutic purposes, and can be used to re-engineer a cell to produce a desired product or improve the production of bio-commodities. (Applicants’ Response filed March 16, 2006, at page 7). If the Office maintains this basis for rejection, Applicants respectfully request clarification of the Office’s remarks at page 4, last paragraph and page 5, first paragraph, because no reasons are provided as to why the above uses do not constitute a practical application.

The claimed invention also falls directly within the scope of patentable subject matter as expressly described in the Examination Guidelines of the M.P.E.P. (e.g., M.P.E.P. §2106

(IV)(B)(1)), and within the Office's current Interim Guidelines published November 22, 2005. Briefly, Applicants respectfully submit that the entire rationale and express language of, for example, M.P.E.P. § 2106 (IV)(B)(1) can be found in Annexes II-V of the Interim Guidelines.

With respect to the Office's assertion that the claimed invention fails to satisfy the requirements of §101 because the method allegedly merely encompasses manipulating sets of data *in silico* with no specific output that is useful, concrete and tangible, Applicants respectfully submit that the claimed invention provides the result of producing an altered network that determines a minimal deletion set which diminishes the capability of the network to produce an output metabolite of interest. In particular, the claims recite forming a flux cone, calculating extreme pathways, eliminating an internal reaction flux thereby producing an altered network and determining if the eliminated flux diminishes the capability of the network to produce an output metabolite of interest. The reaction sets determined to diminish the capability of the network correspond to a minimal deletion set of the network.

A minimal deletion set is described in the application as:

[E]xisting algorithms can be used to calculate the set of extreme pathways that form the conical hull of the solution space corresponding to all feasible steady state flux distributions. . . . From these pathways it is possible to identify sets of reactions that upon removal from the network eliminate the ability of the network to achieve selected objective of interest. Moreover, it is possible to calculate all of these deletion sets using one algorithm that operates on the set of extreme pathways. These minimal deletion sets may be useful for the identification and development of potential protein and genetic targets for antimicrobial drugs and the engineering of microbial strains for bioproduction purposes.

Application at paragraph bridging pages 18-19 (emphasis added).

The application further teaches:

Of particular interest is the ability to use these pathways to identify critical reactions or sets of reactions that are required for the network to reach a particular objective(s). These lethal or minimal sets of reactions and the genes coding for the gene products of these reactions are herein referred to as minimal deletion sets.

When considering the ability of a metabolic network to produce a defined set of metabolic precursors used to generate all of the components of the biomass, these deletion sets correspond to targets or combined targets for antimicrobial therapeutics. When considering the specific production of a metabolite (i.e. amino acid) these sets correspond to reactions that can be deleted to direct the flow of metabolic resources in the cell for the metabolic engineering of an organism.

Application at page 24, para. 3 through page 25 para. 1 (emphasis added).

The above exemplary teachings show that the claimed method does not merely manipulate *in silico* data, as asserted by the Office. The above exemplary teachings show that the claimed method produces a specific output. Moreover, the claims recite the altered network to explicitly claim this inherent output. Further, the output is useful, concrete and tangible. For example, the claimed method provides a minimal deletion set, which correspond to therapeutic or bioproduction targets. Hence, the claimed method constitutes more than mere *in silico* manipulation of data because there is the production of an altered network and the identification of minimal deletion sets as therapeutic and/or bioproduction targets.

With respect to the Office's Interim Guidelines and the interpretation therein of a useful, concrete and tangible result, Applicants submit that the claimed invention satisfies applicable precedent, as set forth above, as well as the Office's Interim Guidelines published November 22, 2005. In particular, the claimed invention satisfies the Office's "useful result" criteria because it has a specific, substantial and credible utility. The utility of the claimed invention is specific to the subject matter claimed, and not general, because the claims recite producing an altered network by eliminating an internal reaction flux and determining whether the eliminated flux is a minimal deletion set because it diminishes the capability of the network to produce a metabolite of interest. Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility, Nov. 22, 2005, section IV.B.2.b., *citing* M.P.E.P. § 2107 (*see also* Revised Interim Utility Guidelines Training Materials at page 5 (1999)). The utility is substantial because it has a real world use, namely, the identification of actual therapeutic and/or bioproduction targets corresponding to the minimal deletion sets. The utility also is credible because there is no reason

for one of skill in the art to question the objective truth of the statement of utility, and it is currently available for use. *Id.* Therefore, the claimed invention produces a useful result under the non-binding Interim Guidelines because it yields a specific, substantial and credible result.

Further, Applicants submit that the claimed invention satisfies the Office's "tangible result" criteria because it yields both the identification of a minimal deletion set and the production of an altered network. Minimal deletion sets correspond to actual therapeutic and/or bioproduction targets. The Interim Guidelines correctly acknowledge that:

The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing.

Interim Guidelines, Nov. 22, 2005, section IV.B.2.b(2) (emphasis added); *see also In re Lundgren* cited in above.

As previously set forth by the Applicants, there is no requirement for a claimed invention to be either tied to a particular machine or to transform a thing to a different state. The Office's own guidelines acknowledged this fact. Accordingly, any rejection based on this requirement is respectfully requested to be withdrawn.

Under this "tangible result" prong of the Office's guidelines, the requirement for a tangible result also must be differentiated from three judicial exceptions to patentability, which are: (1) laws of nature; (2) physical phenomena, and (3) abstract ideas. The guidelines further define the meaning of "tangible" to be opposite of "abstract."

With respect to the first two judicial exceptions above, the invention claims neither a law of nature or a physical phenomena *per se*. Rather, the claimed invention is directed to producing an altered network by eliminating an internal reaction flux, and determining whether the eliminated flux is a minimal deletion set because it diminishes the capability of the network to produce a metabolite of interest. There is no recitation in this claim of merely a law of nature or a physical phenomena. Rather, the method produces an altered network that is diminished in its capability to produce a metabolite. The altered fluxes of such a network correspond to actual therapeutic and/or bioproduction targets. Accordingly, the claimed invention cannot be statutory unpatentable under these two judicial exceptions.

Further, there is nothing in the claimed invention that constitutes a mere abstract idea. First, the claimed invention is more than just an idea because it claims producing an altered biochemical reaction network by eliminating an internal reaction flux and determining whether the eliminated flux diminishes the capability of that biochemical reaction network to produce a metabolite of interest. Hence, the determination or selection of a flux that diminishes biochemical reaction network capability is more than an idea. Rather, it is an actual outcome because it identifies actual therapeutic and/or bioproduction targets.

Second, the claimed invention is not abstract. The term “abstract” is defined as:

[c]onsidered apart from any application to a particular object or specific instance . . . . insufficiently factual . . . . having no reference to a thing or things -- opposed to concrete. . . .  
Expressing a property, quality, attribute, or relation viewed apart from the other characteristics inhering in or constituting an object.

*Webster's Third New International Dictionary, Unabridged.* Merriam-Webster, 2002.

<http://unabridged.merriam-webster.com> (21 Aug. 2006) (emphasis added).

The claimed invention is sufficiently factual because it recites reaction sets and identifies minimal deletion sets of a biochemical reaction network. The reactions are based on a claimed stoichiometric matrix that includes reactions and fluxes of a biochemical network of a cell or organism. Further, the claimed invention is not claimed apart from, or without reference to, a thing or to characteristics in an object because it specifically recites the requisite stoichiometry, reactions and fluxes of a biochemical reaction network of a cell, organism or biological process thereof. Accordingly, the invention is concrete and not abstract because it is sufficiently factual and does not recite purely theoretical ideas detached from a particular object. Therefore, the claimed invention produces a tangible result under the non-binding Interim Guidelines because it does not claim a law of nature, a physical phenomena or merely abstract idea apart from any application to a particular object.

Finally, the claimed invention satisfies the Office's “concrete result” criteria. The Interim Guidelines define this prong as being the opposite of “concrete,” which is “unrepeatable or unpredictable.” Interim Guidelines, Nov. 22, 2005, section IV.B.2.b(3). Applicants

respectfully point out that the invention claims producing an altered network by eliminating an internal reaction flux and determining whether the eliminated flux is a minimal deletion set because it diminishes the capability of the network to produce a metabolite of interest. The minimal deletion sets correspond to actual therapeutic and/or bioproduction targets. Further, Applicants have provided detailed teachings and guidance throughout the application for how to make and use the invention to generate the altered reaction network and how to identify the claimed minimal deletion sets. Therefore, the claimed invention further produces a concrete result under the non-binding Interim.

Thus, in light of any of the applicable precedent as set forth above, Applicants maintain that claims 1-8 satisfy the requirements of §101 for statutory patentable subject matter. The claimed practicable application has the useful, concrete and tangible result of producing an altered network by eliminating an internal reaction flux and determining whether the eliminated flux is a minimal deletion set because it diminishes the capability of the network to produce a metabolite of interest. Accordingly, withdrawal of the rejection is respectfully requested.

#### **Rejections Under 35 U.S.C. § 112**

Applicants respectfully traverse the rejection of claims 1-8 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Office alleges that various phrases recited in claims 1 and 6 are unclear.

Applicants have amended each objected phrase to correspond to the amendments discussed during the personal interview held August 21, 2006. In light of these amendments, Applicants submit that these grounds of rejection are moot and their withdrawal is respectfully requested.



In re Application of:  
Schilling and Letscher  
Application No.: 09/928,191  
Filed: August 11, 2001  
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PATENT  
Attorney Docket No.: UCSD1680

### CONCLUSION

In summary, for the reasons set forth herein, Applicants respectfully submit that the claims clearly and patentably define the invention, and allowance of the claims is respectfully requested. If the Examiner would like to discuss any issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Check number 583818 in the amount of \$225.00 is enclosed as payment for the two-month Petition for Extension of Time fee. No other fee is believed due with this response. However, if a fee is required, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A duplicate copy of the Transmittal sheet is enclosed.

Respectfully submitted,

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